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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
ANGELL, JON E	

ART UNIT	PAPER NUMBER
1635	

DATE MAILED: 01/06/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application N .	Applicant(s)	
	09/732,998	COLLER ET AL.	
	Examin r	Art Unit	
	J. Eric Angell	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 October 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *13-20* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *13-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *23 October 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. This Action is in response to the communication filed on 10/6/03. The amendment has been entered. Claims 1-12 and 21-35 have been cancelled. Claims 13, 16 and 17 have been amended. Claims 13-20 are currently pending in the application and are examined herein.

2. Applicant's arguments are addressed on a per section basis. The text of those sections of Title 35, U.S. Code not included in this Action can be found in a prior Office Action. Any rejections not reiterated in this action have been withdrawn as being obviated by the amendment of the claims and/or applicant's arguments.

Claim Rejections - 35 USC § 112, second paragraph

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 13-20 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Step d) of claim 13 recites, "comparing the level of ***gene expression*** in the indicator cells in the presence ***or*** absence of the agent." (Emphasis added). This phrase renders the claims indefinite for two reasons.

First, it appears that the word "or" should be changed to "and" because it is unclear how to compare in the presence or absence of the agent. It is only clear how to compare in the presence and in the absence of the agent.

Second, the phrase, "the level of gene expression" is unclear because it is unclear as to which gene the level of expression is measured. That is, it is unclear if the level of one particular gene, certain specific genes, or all genes is determined. Claims 14-20 are dependent claims and are therefore, rejected for the same reasons.

Additionally, Claim 16 is unclear because although the claim is dependent on claim 13 (as evidenced by the phrase "The method of claim 13") it is unclear if the phrase "gene expression" in line 1 is referring to the level gene expression evaluated in claim 13 or if the "gene expression" evaluated in claim 16 is separate from, or in addition to the gene expression evaluated in claim 13. The claim should be amended to make it clear which gene expression is evaluated in claim 16.

Claim Rejections - 35 USC § 112, first paragraph

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 13-20 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 USC 112, first paragraph, have been described by the court in *In re Wands*, 8 USPQ2d 1400 (CA FC 1988).

Wands states on page 1404,
"Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in Ex parte Forman. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims."

The instant claims are drawn to a method for identifying an agent that regulates MYC dependent transcriptional regulation of gene expression using cells that have been modified to express a chimeric receptor comprising Myc and a hormone ligand-binding domain. It is noted that, as written, it is required that the method absolutely identifies if an agent is a regulator of MYC-dependent transcriptional regulation of gene expression. However, the claimed method would not necessarily positively identify a test agent as a regulator of MYC dependent transcriptional regulation of gene expression and further experimentation would be required in

order to verify that the result of the claimed method was correct. Therefore, the claimed method is not enabled. An analysis of the Wands factors is below.

The nature of the invention

The instant claims are drawn to a method for identifying an agent that regulates MYC dependent transcriptional regulation of gene expression using cells that have been modified to express a chimeric receptor comprising Myc and a hormone ligand-binding domain.

The breadth of the claims

The claims are broad, and encompass a method using a chimeric protein comprising MYC and a hormone ligand-binding domain. It is noted that the superfamily of hormone receptors (i.e., those receptors that have hormone ligand-binding domains) includes nearly 40 different receptors for thyroid and steroid hormones, retinoids and vitamin D as well as different "orphan" receptors which bind unknown ligands (Aranda et al., Physiol. Rev. 2001; see Abstract; p. 1270, second column; and Table 1, p. 1272).

The unpredictability of the art and the state of the prior art

As mentioned above, the claims encompass an assay system that utilizes a chimeric molecule comprising MYC and a hormone ligand-binding domain wherein the appropriate hormone is applied to the cell(s) comprising the chimeric molecule. Therefore, the claims encompass using a Myc/estrogen receptor chimera comprising MYC and a hormone-binding domain for estrogen.

It is noted that the claims also encompass using this assay system to evaluate the effect of a test agent on MYC's ability to transcriptionally regulate the expression of genes. In order for the claimed method to work, it is imperative that the results are solely due to the effect of the test on MYC. However, it is possible that the results of the claimed method could be caused by factors other than the test agent working on MYC. For instance, Littlewood (cited as reference AX2 in the IDS form 1449) teaches,

> "A number of proteins have been rendered functionally oestrogen-dependent by fusion with the hormone-binding domain of the oestrogen receptor. There are, however, several significant disadvantages with such fusion proteins. First, their use in cells in vitro requires phenol red-free medium and laborious stripping of steroid hormones from serum in order to avoid constitutive activation. Secondly, control of oestrogen receptor fusion proteins in vivo is precluded by high endogenous levels of circulating oestrogens. Thirdly, the hormone-binding domain of the oestrogen receptor functions as a hormone-dependent transcriptional activation domain making interpretation of fusions with transcription factors problematical." (See abstract).

Therefore, it is clear from the teachings of Littlewood that there are a number of problems with the claimed method. Specifically, using a chimera comprising a hormone-ligand domain is susceptible to activation from hormones (such as estrogen) present in media used to culture the cells. Second, Littlewood teaches that hormone binding domains (including the estrogen binding domain) functions as a hormone-dependent transcription activation domains making interpretation of fusions with transcription factors problematical.

Furthermore, there are a number of problems with the claimed assay system that would be apparent to one of skill in the art. For instance, the hormone or test agent used in the assay could directly activate/inactivate expression of the genes independent of MYC functioning, thus giving a false positive result. However, the hormone used to activate the chimeric molecule could activate hormone receptors present in the cell. Furthermore, the claim encompasses testing

compounds wherein the test compounds can be transcription factors. When a transcription factor is tested in the claimed assay system it is possible that the transcription factor could activate or inactivate its target genes without working on the chimeric molecule. In this case, the claimed assay would indicate that the test agent was a regulator of MYC-dependent transcriptional regulation of gene expression, when, in fact, it is not. Additionally, it would be readily apparent to one of skill in the art that the test agent could effect the interaction of the hormone for the hormone-binding domain of the chimera. Again, the claimed method would improperly identify the agent as modulator of MYC function. Therefore, it is clear that there are a number of different problems associated with the claimed method that prevent the method from being able to whether a test agent is a regulator of MYC function without performing additional experimentation in order to verify the results of the claimed method.

Working Examples and Guidance in the Specification

It is noted that the specification does not include any examples that show that the claimed method has been used to actually identify a regulator of MYC dependent transcriptional regulation of gene expression.

Quantity of Experimentation

Additional experimentation would be required in order for the claimed method to be able to identify an agent as a regulator of MYC's transcriptional regulation of gene expression function. For instance, the additional experimentation would have show that the claimed method could identify regulators of MYC's transcriptional regulation function in light of the problems

indicated in the prior art, as well as the problems that would be apparent to those of skill in the art, as indicated above. Considering the problems indicated above, is highly unlikely, absent evidence to the contrary, that the claimed method could absolutely identify an agent as a regulator of MYC function, as indicated in the claims.

Level of the skill in the art

The level of the skill in the art is deemed to be high.

Conclusion

Considering the high degree of unpredictability recognized in the art, the breadth of the claims, the lack of a working example indicating that the claimed method can absolutely identify an agent as a MYC regulator, the limited guidance provided in the specification; and the high degree of skill required to practice the claimed method, it is concluded that the amount of experimentation required to be able to practice the broadly claimed method is undue.

Response to Arguments

7. Applicant's arguments, see the response filed 10/6/03, with respect to the rejection(s)of claim(s) under 35 USC 112, first and second paragraphs have been fully considered and are persuasive. Therefore, the rejection has been withdrawn. However, upon further consideration, a new ground(s) of rejection is made for the reasons indicated herein.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to J. Eric Angell whose telephone number is (703) 605-1165. The examiner can normally be reached on M-F (8:00-4:30).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John L. LeGuyader can be reached on (703) 308-0447. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

DAVE T. NGUYEN
PRIMARY EXAMINER

J. Eric Angell
Art Unit 1635